ORIGINAL ARTICLE

The natural course of the paravertebral muscles after the onset of osteoporotic vertebral fracture

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Received: 11 November 2019 /Accepted: 6 February 2020 /Published online: 14 February 2020 \odot International Osteoporosis Foundation and National Osteoporosis Foundation 2020

Abstract

Summary This study revealed the change in the paravertebral muscles in patients with osteoporotic vertebral fracture. Increased pain is likely to be the driver for reduced activity, reduced activities of daily living, and consequent increase in fat infiltration of the paravertebral muscles, assumed to be secondary to reduced activity level or, conversely, partial immobilization.

Introduction To reveal the time courses and impact of the paravertebral muscles (PVMs) on the healing process of osteoporotic vertebral fractures and risk factors for PVM decrease.

Methods Consecutive patients with symptomatic osteoporotic vertebral fractures were enrolled in 11 hospitals. At enrollment and 3- and 6-month follow-up, PVMs, including the multifidus and erector spinae, were examined using magnetic resonance imaging (MRI). The PVM cross-sectional area (CSA) and fat signal fraction (FSF) were measured at L3. Low back pain (LBP), activities of daily living (ADLs), and risk factors for PVM decrease at the 6-month follow-up were investigated. PVM decrease was defined as > 1 standard deviation decrease of the CSA or > 1 standard deviation increase of the FSF.

Results Among 153 patients who completed the 6-month follow-up, 117 (92 women, 79%) had MRI of L3 at enrollment and 3 and 6-month follow-up (mean age at enrollment, 78.5 years). The CSA did not change 6 months from onset (p for trend = 0.634), whereas the FSF significantly increased (p for trend = 0.033). PVM decrease was observed in 30 patients (26%). LBP was more severe, and delayed union was more frequent in patients with PVM decrease $(p = 0.021$ mixed-effect model and $p = 0.029$ chisquare test, respectively). The risk factors for PVM decrease were ADL decline at the 3-month follow-up (adjusted odds ratio = 5.35, $p = 0.026$).

Conclusion PVM decrease was significantly related to LBP and delayed union after osteoporotic vertebral fracture onset. ADL decline at the 3-month follow-up was a risk factor for PVM decrease. Therefore, restoring ADLs within 3 months after onset is important.

Keywords Magnetic resonance imaging . Osteoporotic vertebral fractures . Paravertebral muscle . Risk factor

Electronic supplementary material The online version of this article ([https://doi.org/10.1007/s00198-020-05338-8\)](https://doi.org/10.1007/s00198-020-05338-8) contains supplementary material, which is available to authorized users.

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Introduction

Osteoporotic vertebral fracture is a common disease with a prevalence of approximately 50% in 80-year-old Japanese female patients [\[1\]](#page-5-0). Osteoporotic vertebral fracture has a significant impact on the health status of elderly people and is a very important health issue in the aging society. Clinical osteoporotic vertebral fractures can result in a decline in the patients' quality of life and survival rate $[2, 3]$ $[2, 3]$ $[2, 3]$ $[2, 3]$ $[2, 3]$. On the other hand, there is no universal treatment strategy for osteoporotic vertebral fractures. To decrease pain and immobility in acute vertebral fracture, the use of spinal orthoses becomes inevitable [\[4](#page-5-0)]. However, there is no apparent difference in the compression ratio, bony union rate, and clinical outcome according to the conservative treatment [\[5,](#page-5-0) [6\]](#page-5-0). Therefore, it is very important to reveal further the risk factors for poor outcome after osteoporotic vertebral fractures, and many studies have investigated factors related to poor outcome [\[5,](#page-5-0) [7](#page-5-0), [8\]](#page-5-0).

The paravertebral muscles (PVMs) have a substantial role in low back pain (LBP), sagittal balance, and quality of life [\[9](#page-5-0)–[11\]](#page-6-0). Concomitant with the loss of muscle, aging also results in progressive bone loss, leading to bone fragility and increased risk for osteoporosis and fractures [[12\]](#page-6-0). Regarding osteoporotic vertebral fractures, Sinaki et al. [\[13\]](#page-6-0) demonstrated that individuals who performed spinal flexion and bending exercises increased their risk of developing further vertebral compression fractures. In contrast, another study showed that back strengthening exercises are helpful for decreasing the risk of further osteoporotic vertebral fractures [\[14](#page-6-0)]. Exercise can be beneficial for reducing the occurrence of vertebral fracture, improving disequilibrium, and decreasing the risk of falls [\[15\]](#page-6-0). However, the change in the PVMs after osteoporotic vertebral fracture injury remains unclear. The PVMs may also have a substantial role in the healing process of fractured vertebrae and patient's outcome. A better understanding of the change in the PVMs after osteoporotic vertebral fractures is critical to the development of more effective strategies to improve osteoporotic vertebral fracture treatment. However, the natural course of changes in the PVMs following osteoporotic vertebral fractures is unclear. Kim et al. [\[16](#page-6-0)] demonstrated that osteoporotic patients with osteoporotic vertebral fractures showed reduction of CSA and increased intramuscular fat infiltration compared to those without osteoporotic vertebral fractures. So et al. [\[17\]](#page-6-0) showed the increase of fatty infiltration at L3. However, they did not evaluate the time course after the onset of osteoporotic vertebral fractures. The purpose of this study was to reveal the time courses and impact of the PVMs on the healing process of osteoporotic vertebral fractures and the risk factors for the decrease.

This was a multicenter cohort study in 11 institutions [[18](#page-6-0)]. From 2012 to 2015, 153 patients with symptomatic

Methods

osteoporotic vertebral fractures were followed up for 6 months after the onset of osteoporotic vertebral fractures. The inclusion criteria were age of > 65 years, diagnosis of a recent osteoporotic vertebral fracture, and back pain onset within 2 weeks prior to presentation. The exclusion criteria were pathological fractures, multiple fractures, malignant cancer, dementia, and high-energy injury.

Demographic data included age, sex, and body mass index (BMI). BMI was computed as the ratio of the body mass in kg divided by the height in m^2 . The severity of pain was subjectively assessed by the patients with a visual analog scale (VAS), which was based on the average level of back pain that the patient had felt in the previous week. To evaluate the patients' activities of daily living (ADLs), we used the criteria proposed by the long-term care insurance system of the Japanese Health and Welfare Ministry for evaluation of the degree of independence of disabled elderly individuals [\[8](#page-5-0)]. In rank J, although some disability is present, daily life is almost independent and patients can leave the home without assistance from other individuals; in rank A, patients live independently indoors but require assistance to leave the home; in rank B, patients require some assistance living indoors and spend most of the day in bed but are able to sit up, and in rank C, patients spend all day in bed and require assistance with urination/defecation, dressing, and eating. We divided the ranks into two groups, that is, J, A (dependent or requires assistance to leave home) and B, C (bedridden or nearly bedridden). Magnetic resonance imaging (MRI), radiographic examinations, VAS, and ADLs were evaluated at enrollment and at 1, 3, and 6 months after the onset.

During treatment, 30% of patients wore tailor-made hard corsets, 62% wore tailor-made elastic corsets, 4% wore readymade elastic corsets, and 4% did not wear a corset. Mobilization to an erect position and ambulation were basically allowed immediately when the brace had been applied. Medication includes common analgesics, such as acetaminophen and non-steroidal anti-inflammatory drugs. Rehabilitation was performed during admission only for patients who were admitted. The rehabilitation focused on early activity, not according to any study protocol. No back-muscle exercise was prescribed during the study period.

Imaging assessment

For measuring the CSA and fatty infiltration of the lumbar paraspinal muscles, MRI was recommended because of the higher reliability and absence of radiation exposure compared to computed tomography [\[19\]](#page-6-0).

At the time of enrollment and at the 3- and 6-month followups, the patients were examined using plain radiography and spine MRI. MRI was carried out with 1.5-T MRI scanners. The multifidus (MF) and erector spinae (ES) including the longissimus and iliocostalis were identified as the medial-to-

lateral PVMs. The border between the MF and ES was scouted from the mammillary processes [\[20\]](#page-6-0). The crosssectional area (CSA) was calculated by the average of the left and right PVM regions of interest of the axial T2-weighted image. The fat signal fraction (FSF) was calculated as the ratio of signal fat/CSA \times 100. The CSA and FSF at the superior endplate of L3 were measured using a software program (Horos, version 2.0.1, Horos Project). PVM decrease was defined as > 1 standard deviation (SD) decrease in the CSA (0.9 cm^2) or > 1 SD increase in the FSF (5.7%) at the 6month follow-up compared with the values at the time of injury.

Plain radiographs were assessed on the sagittal view in both the supine and weight-bearing positions. The relative height of the anterior wall (%) was calculated by the following formula: $[2 \times$ affected vertebral height / (lower vertebral height + upper vertebral height)] \times 100 [[18](#page-6-0)]. When either the cranial or caudal adjacent vertebral body was deformed due to an old fracture, the vertical height of the anterior wall of the fractured vertebral body was divided by the vertical height of the anterior wall of the undeformed adjacent vertebral body. Delayed union was defined by a recognizable intravertebral cleft on plain radiography at the 6-month follow-up. Dual-energy xray absorptiometry was used to measure the bone mineral density (BMD) of the mean femoral neck at the time of enrollment.

Data analysis

Jonckheere's trend test was used to evaluate the trend of the CSA and FSF of ES, MF, and total PVM. To establish whether there was a significant difference in the VAS score of back pain, CSA, and FSF of ES, MF, and total PVM between the PVM decrease and non-decrease groups, a restricted maximum likelihood, mixed-model regression was used. T test was used for continuous variables. Either the chi-square test or Fisher's exact test was used to compare the categorical variables. The odds ratio (OR) of each variable for PVM decrease was calculated using a logistic regression model adjusted for age, sex, BMI, old osteoporotic vertebral fractures, admission, institution, and ADLs at each time point, or delayed union. Demographic data and those with a p value of \lt 0.1 in the univariate analysis were included in the multivariate analysis. The variable of delayed union was entered in the model, but that of angular motion between the supine and sitting positions was not because of multiple collinearity. Additionally, the variables of ADLs, VAS of back pain, and delayed union were separately inserted into the model because of multiple collinearity. Statistical test results were considered significant at $p < 0.05$. All p values were two-sided. All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Among the 153 eligible patients, 40 patients were excluded because of the lack of MRI data including axial T2-weighted image at L3. As a result, 117 patients (92 women and 25 men) with a mean age of 78.5 years (standard deviation 7.4) were finally analyzed.

Regarding the trend of the CSA and FSF, there were no trends in the CSA of ES, MF, and total PVM (Table 1). On the other hand, the FSF in both ES and MF showed an increasing tendency from $42.3\% \pm 7.8\%$ and $53.0\% \pm 8.9\%$ to $44.2\% \pm$ 8.3% and 55.4% \pm 9.3%, respectively, for 6 months ($p = 0.078$) and 0.055, respectively). The FSF of total PVM showed a significant increase from 47.7 to 49.8% for the period ($p =$ 0.033). The mean change in the CSA and FSF of total PVM was $-0.2 \text{ cm}^2 \pm 0.6 \text{ cm}^2$ and $2.1\% \pm 3.6\%$, respectively. There were 30 patients with PVM decrease at the 6-month followup.

There were no differences in age, BMI, brace duration, BMD, and fractured level between the PVM decrease and non-decrease groups (Table [2](#page-3-0)). The male proportion was significantly lesser in the PVM decrease group ($p = 0.023$). Old

Table 1 Trend of the paravertebral muscle for 6 months

	Mean	SD	p for trend*
CSA of ES (cm ²)			
At enrollment	11.2	(2.6)	0.609
3 months	11.2	(2.5)	
6 months	11.0	(2.6)	
CSA of MF $(cm2)$			
At enrollment	3.5	(1.1)	0.795
3 months	3.5	(1.2)	
6 months	3.5	(1.2)	
FSF of ES $(\%)$			
At enrollment	42.3	(7.8)	0.078
3 months	44.5	(8.1)	
6 months	44.2	(8.3)	
FSF of MF $(\%)$			
At enrollment	53.0	(8.9)	0.055
3 months	55.1	(9.3)	
6 months	55.4	(9.3)	
CSA of total PVM $(cm2)$			
At enrollment	14.7	(3.1)	0.634
3 months	14.8	(3.1)	
6 months	14.5	(3.1)	
FSF of total PVM (%)			
At enrollment	47.7	(7.3)	0.033
3 months	49.8	(7.6)	
6 months	49.8	(7.8)	

CSA cross-sectional area, ES erector spinae, MF multifidus, FSF fat signal fraction, PVM paravertebral muscle

*p values were calculated using Jonckheere's trend test

Table 2 Comparison of demographic and radiological data at baseline between the PVM decrease and non-decrease groups

PVM, paravertebral muscle; BMI, body mass index; BMD, bone mineral density; OVF, osteoporotic vertebral fracture

 $*p$ values were calculated by using t test, chi-square test, or Fisher's exact test

osteoporotic vertebral fractures were more frequently observed in the PVM decrease group (50% vs. 28%, respectively, $p = 0.042$,). Table 3 shows that the VAS score of back pain

Table 3 Time course of back pain and radiological findings for 6 months between the PVM decrease and non-decrease groups

	PVM decrease $n = 30$	Non-decrease $n = 87$	p value*
VAS of back pain			
At enrollment	74.1 (18.9)	70.1 (21.2)	
1 month	37.6 (27.2)	40.9 (24.5)	
3 months	35.9(25.4)	27.0 (27.8)	
6 months	34.9 (32.8)	20.4 (22.0)	0.021
Compression ratio			
At enrollment	85.0 (15.5)	82.0 (12.5)	
1 month	76.3 (16.1)	68.9 (17.5)	
3 months	64.3 (18.4)	63.2(19.3)	
6 months	60.9 (21.9)	60.0(21.1)	0.545
Kyphotic angle			
At enrollment	6.6(4.6)	6.9(6.2)	
1 month	12.4(6.7)	8.7(6.0)	
3 months	14.0(7.2)	12.0(7.5)	
6 months	15.4 (7.9)	14.2(8.7)	0.456
Angular motion between the supine and sitting positions			
At enrollment	4.6(3.1)	5.2(3.9)	
1 month	6.0(3.7)	3.8(5.1)	
3-months	4.6(4.1)	2.6(3.6)	
6 months	3.2(4.8)	1.7(3.6)	0.013
Delayed union (yes)	10(33%)	12(14%)	0.029

PVM paravertebral muscle, VAS visual analogue scale

*p values were calculated by mixed-effect model or chi-square test

was significantly higher in the PVM decrease group throughout the study period ($p = 0.021$). Compression ratio and kyphotic angle of fractured vertebrae were not different between the two groups. However, the angular motion between the supine and sitting positions was significantly higher in the PVM decrease group $(p = 0.013)$. Delayed union was more frequently observed in the PVM decrease group than in the non-decrease group (33% vs. 14% , $p = 0.029$). Regarding ADLs, the status of "bedridden or nearly bedridden" was more frequently observed in the PVM decrease group at the 3 month follow-up (38% vs. 15%, $p = 0.019$), whereas no significant differences were found at the other time points (Table [4](#page-4-0)).

The results of the multivariate logistic regression model are listed in Table [5.](#page-4-0) Compared with the status of "dependent or requires assistance to leave home," patients with the status of "bedridden or nearly bedridden" at the 3-month follow-up displayed a fourfold increase of the risk for PVM decrease (OR = 5.35; 95% CI, 1.23–23.34). Patients who had delayed union at 6-month follow-up also increased the OR for PVM decrease (OR = 4.12; 95% CI, 1.16–14.71). The admission significantly reduced the risk for PVM decrease ($OR = 0.24$; 95% CI, 0.06–0.97). VAS of back pain at the 6-month followup was associated with PVM decrease ($OR = 1.24$; 95% CI, 1.02–1.49). A typical case was shown in supplementary figure. The case showed the increase of the FSF at 3- and 6 month follow-up.

Discussion

This study is the first to reveal the natural course of the PVMs after the injury of osteoporotic vertebral fractures. The CSA Table 4 Comparison of activities of daily living between the PVM decrease and non-decrease groups

PVM paravertebral muscle, ADL activities of daily living

*p values were calculated by chi-square test

did not change for 6 months, but the FSF significantly increased. CSA might be unlikely to reflect the early change in the PVMs compared with the FSF. This result may be con-sistent with the age effect of PVM change. Shahidi et al. [\[21\]](#page-6-0) quantified changes in the CSA and FSF with age in men and women with lumbar spine pathology. There was no change in CSA with age in either sex $(p > 0.05)$, but there was an increase in the FSF with age in the ES and MF muscles in both sexes ($p < 0.001$). Hebert et al. [[10\]](#page-6-0) described that fatty infiltration appears earlier in individuals with a low back disorder.

Table 5 Adjusted odds ratios for PVM decrease

	aOR ^a	95%CI	<i>p</i> value
Age	1.01	$0.92 - 1.11$	0.821
Sex (female)	13.09	1.15-148.76	0.038
BMI (kg/m^2)			
< 18.5	3.10	$0.30 - 32.14$	0.343
$18.5 - 25.0$	ref.		
> 25.0	0.54	$0.11 - 2.66$	0.452
Old OVF (yes)	0.51	$0.15 - 1.79$	0.294
Admission (yes)	0.24	$0.06 - 0.97$	0.046
Delayed union (yes)	4.12	1.16-14.71	0.029
ADL (bedridden or nearly bedridden)			
1 month	1.86	$0.53 - 6.55$	0.337
3 months	5.35	$1.23 - 23.34$	0.026
6 months	3.87	$0.74 - 20.22$	0.108
VAS of back pain (per 1 point)			
At enrollment	1.04	$0.81 - 1.35$	0.735
1 month	0.94	$0.75 - 1.16$	0.540
3 months	1.14	$0.94 - 1.37$	0.180
6 months	1.24	$1.02 - 1.49$	0.028

PVM paravertebral muscle, aOR adjusted odds ratio, BMI body mass index, OVF osteoporotic vertebral fracture, ADL activities of daily living a Odds ratios were adjusted for age, sex, BMI, old OVF, admission, institution, and delayed union, ADL at each time point, or VAS at each time point

In addition, a cross-sectional study [[22\]](#page-6-0) demonstrated that paraspinal fat infiltration, but not muscle CSA, was associated with disability and structural abnormalities in the lumbar spine. Therefore, the FSF might be more useful when observing PVM change. Fatty infiltration in the muscles could be associated with mechanisms, such as generalized disuse, chronic denervation, and aging [[23](#page-6-0)].

LBP is reported as a risk factor for PVM decrease. Although Paalanne et al. [\[24\]](#page-6-0) evaluated the PVMs of 554 young adults (18–21 years of age) and showed that the CSA of the lumbar paraspinal muscles did not correlate with symptom severity, a significantly higher fat content in the MF muscle was found in patients with chronic LBP than in asymptomatic volunteers [\[25](#page-6-0)]. D'hooge et al. [\[22\]](#page-6-0) showed that fatty infiltration in the lean muscle tissue was increased, without alterations in muscle size or macroscopic fat deposition during remission of LBP, and they demonstrated the positive correlation between fatty infiltration and LBP episode frequency. In the current longitudinal study, patients with PVM decrease showed an increase in LBP. Moreover, Hori et al. [[9\]](#page-5-0) demonstrated that trunk muscle mass was significantly associated with quality of life and VAS score for LBP. Our study showed that back pain at the 6-month follow-up was associated with PVM decrease. However, the causality was unclear.

So et al. [\[17](#page-6-0)] demonstrated in a cross-sectional study that fat infiltration of low back extensor muscle was increased in patients with osteoporotic vertebral fractures. Kim et al. [\[16](#page-6-0)] also conducted a cross-sectional study to investigate the PVM influence on postmenopausal osteoporotic vertebral fractures. Postmenopausal osteoporotic vertebral fractures were associated with reduction of CSA and increased fat infiltration [[16\]](#page-6-0). However, the causality of PVM decrease and osteoporotic vertebral fracture was unclear. The current study demonstrated that the FSF deteriorated from 47.7 to 49.8% for 6 months. This change is greater than one in the FSF of the PVMs, from 28.8 to 31.6%, during 9 years among individuals aged 40 years [\[26](#page-6-0)], while there has been no report revealing serial changes in the PVMs in the elderly. Our study suggests that the FSF

increased after osteoporotic vertebral fractures, indicating that osteoporotic vertebral fractures result in PVM decline, although our study did not demonstrate whether PVM decline increased the risk of osteoporotic vertebral fracture or not.

Movement of vertebrae requires the PVMs to contract and work against the levers of an internal skeleton. Disuse or unweighting of the muscle-bone unit in immobilized individuals results in a dramatic loss of bone and muscle mass [[12\]](#page-6-0). Muscular atrophy of extremities regularly occurs as a consequence of immobilization or disuse [[27\]](#page-6-0). To avoid atrophy of supported back muscles, the use of spinal supports may need to be discontinued as soon as pain subsides [[28](#page-6-0)]. Significant changes in muscle weight and fiber size are reported in the first week of immobilization. The patients with osteoporotic vertebral fractures are not able to move the spine causing disuse atrophy of the PVMs. Osteoporotic vertebral fractures also alter neuromuscular patterns in individuals who have sustained vertebral fracture compared to those who have no history of vertebral fracture, and this may be interpreted as one of the sequelae of vertebral fractures [\[29](#page-6-0)]. Our study showed that ADL decline (bedridden or nearly bedridden) for 3 months was associated with PVM decrease. However, ADL decline at the 6-month follow-up was not associated with PVM decrease. The reason might be that the patients with poor ADLs at the 6-month follow-up had poorer ADLs before injury, which might be linked to less change. On the other hand, patients who were admitted to the hospital had reduced risk for PVM decrease. This might indicate that rehabilitation prevented disuse atrophy despite immobilization by brace treatment for 3 months.

There are several limitations in this study. First, we did not check the other risk factors including low levels of vitamin D associated with high levels of parathyroid hormone, low levels of anabolic hormones in men and menopause in women, malnutrition, and frailty [\[22](#page-6-0)]. These factors could be at a higher risk for PVM reduction. Second, this study did not include controls who had no osteoporotic vertebral fractures. It was unclear that PVM decrease was dependent on aging or osteoporotic vertebral fractures. Third, nerve root compression was one of the risk factors for fat infiltration, but radiculopathy was not assessed. Finally, a prior episode of LBP was not assessed in this study. If chronic LBP was present, the course of LBP after osteoporotic vertebral fractures might be influenced by the other causes.

In conclusion, the FSF significantly increased for 6 months after osteoporotic vertebral fracture injury. ADL decline at the 3-month follow-up was a risk factor for PVM decline. LBP at the 6-month follow-up was higher in patients with PVM decline. Another treatment strategy should be considered in patients with ADL decline at the 3-month follow-up.

Funding information This study was funded by the Grant of Japan Orthopedics and Traumatology Research Foundation (Grant no. 270).

Compliance with ethical standards

Conflict of interest None.

Ethical approval This study was approved by the Ethics Committee of Osaka City University. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all participants included in the study.

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